REMARKS

The Examiner states that claim 18 is both withdrawn and examined in the Office Action. Applicants, from the restriction requirement, assume that the Examiner meant that claims 1-17 are examined on the merits of the Office Action. Therefore, Claims 1-17 and 30-34 constitute the pending claims in the present application. The Examiner has withdrawn from consideration claims 18-29. Applicants have amended claim 2 to remove a second period at the end of the claim.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Specification

The Examiner objects to the disclosure as allegedly containing an embedded hyperlink and/or other form of browser executable code. In response, Applicants have amended the specification to remove the hyperlink.

Claims Rejections

Rejection based on 35 U.S.C. 101. The Examiner has rejected claims 1-17 and 30-34 under 35 U.S.C. 101 as being directed to non-statutory subject matter because the claims do not produce a tangible result. Applicants traverse this rejection.

The Examiner cites section 2106 of the M.P.E.P. which states, "The tangible requirement does not necessarily mean that a claim must either be tied to a particular machine or apparatus or must operate to change articles or materials to a different state or thing. However, the tangible requirement does require that the claim must recite more than a 35 U.S.C. 101 judicial exception, in that the process claim must set forth a *practical application* of that judicial exception to *produce a real-world result*."

Applicants respectfully submit that a practical application to produce a real-world result is the determination of the "probability that continued treatment of the subject with the regimen will result in a favorable outcome" contained in step (vi) of the pending independent claims.

This result is not qualitatively or quantitatively different from the result of a screening assay to identify compounds having a particular activity or mode of action, which assays are routinely deemed patentable subject matter. In both cases, the result of the method is gaining specific information that can be directly applied in useful ways, e.g., to predict the result of a specific future action. Here, the information as to the probability that continued treatment of the subject will result in a favorable outcome can be used to assess, broadly, the value of the treatment regimen in human therapy of subjects with a particular condition, or, specifically, whether treatment of a particular patient should continue or an alternate therapy should be sought. The advantage of the claimed methods is that this information can be gained earlier in the treatment process than, for example, waiting for the ultimate resolution of the condition being treated, e.g., curing or remission of the condition. It hardly needs to be said that it is useful to have this information earlier in the treatment process, and that improving the treatment of human disease is a real-world application with practical value.

Applicants respectfully point out that the entire section of the MPEP relied on by the Examiner concerns claims directed to "abstract ideas, laws of nature, and natural phenomena". It is hard to imagine to which of these categories the Examiner believes the claimed invention might belong. The claimed method clearly involves steps that produce physical transformation - administering medical treatment to a patient, for example. If the Examiner wishes to maintain this rejection, Applicants respectfully submit that a prima facie case be more clearly laid out on the record, as required by MPEP 2106 IV.D. The rejection currently formulated by the Examiner does little more than restate the law and make generalized and unsupported statements about the subject matter of the claims. In light of the above remarks, Applicants respectfully request reconsideration and withdrawal of this rejection

Rejection based on 35 U.S.C. 102(b). The Examiner has rejected claim 1 under 35 U.S.C. 102 (b) as being anticipated by Haybittle et al., British Journal of Cancer, 1982, volume 45, pages 361-366 ("Haybittle") in light of Zhou, American Statistics, May 2001, volume 55, pages 153-155 ("Zhou"). Applicants traverse this rejection to the extent that it is maintained over the claims as amended.

Haybittle describes a method for the study of prognostic factors (including age, menopausal status, tumor size and grade, and oestrogen-receptor (RE) content) in a series of 387

female patients afflicted with breast cancer and treated by a mastectomy and triple-node biopsy. (Haybittle, abstract). Haybittle uses survival time of the patients as a measure of the outcome of the treatment. (Haybittle, p. 362, column 1). Measurements of these factors are taken before and after treatment. Data generated from this method is analyzed using a procedure described in Zhou. This analysis is used to derive a prognostic index (I) for each patient. These I values were then used to group patients with regard to their specific prognosis.

Conversely, the pending claims define a method for monitoring the effectiveness of a regimen for the treatment of *an ocular disease,* comprising (i) obtaining, from a subject, one or more measurements selected from self-reported data and behavioral, genetic, neurological, biochemical, and physiological measurements; (ii) *treating said subject*, or a different subject, *with said regimen for a selected period of time*; (iii) obtaining from a subject who has been treated with the regimen, one or more measurements selected from self-reported data and behavioral, genetic, neurological, biochemical and physiological measurements; (iv) determining changes in the measurements induced by the regimen, by comparing the measurements obtained in (i) with the measurements obtained in (iii); (v) comparing said measurements or changes in the measurements, or both, to a signature, said signature representing probability relationships between one or more predictor variables and one or more clinical outcomes for said disease; and (vi) determining, from the comparison in step (v), a probability that *continued treatment of the subject with the regimen will result in a favorable clinical outcome.* Haybittle does not disclose nor suggest using its prognostic index to monitor the effectiveness of a regimen for treatment of an ocular disease. Breast cancer is the sole disease contemplated by Haybittle.

In addition, continued treatment (step vi) of a subject in Haybittle to result in a favorable outcome is not a possibility, as mastectomy is a treatment/regimen that cannot be continued or discontinued. The Examiner contends that the treatment/regimen of step (ii) exists in Haybittle as the adjuvant chemotherapy administered in addition to the mastectomy and biopsy treatments. However, Haybittle later stipulates that investigation of the application of the prognostic index excludes those patients treated with adjuvant chemotherapy (Haybittle, p. 363). Therefore, the only treatment considered by Haybittle in the context of a method bearing any correlation to the pending claims is mastectomy. Mastectomy is not a regimen that can be applied for a specified

period of time as in step (ii) of the pending claims. A mastectomy is a surgical operation that is immediate and permanent and is therefore is outside the scope of step ii of the pending claims.

In light of the above arguments, Applicants traverse the rejection and maintain that the claims are novel as amended because Haybittle does not teach each and every limitation of the pending claims. Applicants respectfully request the Examiner withdraw the rejection based on Haybittle.

Rejection based on 35 U.S.C. 103. Claims 1-3 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haybittle as evidenced by Zhou in view of Augsburger et al., British Journal of Opthamology, 1989, vol. 73, p. 911-917 ("Augsburger") in view of Smerhovsky et al., Environmental Health Perspectives, January 2001, vol. 109, p. 41-45 ("Smerhovsky"). Applicants traverse this rejection to the extent that it is maintained over the claims as amended.

Pursuant to MPEP 2142, "To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicants' disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)."

Augsburger describes a follow up of 197 patients with melanotic choroidal lesions, in which all patients were left untreated for a five-year interval. Individual clinical parameters, predictive of lesions enlargement, were observed. The best combination of these parameters for prediction of lesion enlargement was identified by multivariate Cox regression analysis. These parameters consisted of thickness of the lesion, and retinal detachment.

While Augsburger describes steps similar to (i) of the pending application, it neither mentions nor suggests a method for *monitoring the effectiveness of a regimen* for treatment of a disease. In fact, there is no suggestion of a regimen or treatment within Augsburger. Furthermore, Augsburger does not teach nor suggest determining from a comparison a

probability that *continued treatment* of the subject with a regimen will result in a favorable outcome.

Smerhovsky describes a cytogenic analysis to test the association between frequency of chromosomal aberrations and subsequent risk of cancer. Smerhovsky does not teach nor suggest a method for monitoring the effectiveness of a regimen for treatment of any disease, no less an *ocular disease* wherein, a determination is made from a comparison of measurements taken before and after a treatment regimen, a probability that *continued treatment of a subject with said regimen* will result in a favorable outcome. Moreover, Smerhovsky is silent with regard to any type of treatment or regimen. In addition, Smerhovsky does not provide motivation to combine with the teachings of either Augsburger or Haybittle.

As discussed above, Haybittle does not teach a method for monitoring the effectiveness of a *regimen that is administered for a selected period of time* for treatment of an *ocular disease*, wherein a determination of a probability that *continued treatment of a subject with said regimen* will result in a favorable clinical outcome is made from a comparison of measurements taken before and after the treatment regimen. While Augsburger is directed toward the use of prognostic parameters for an ocular disease, neither Augsburger nor Smerhovsky discloses a regimen that is administered for a selected period of time (step ii) or the determination of a probability that continued treatment with said regimen will result in a favorable clinical outcome (step vi). Therefore, Haybittle in view of Augsburger in view of Smerhovsky does not teach or suggest all of the claimed limitations of the subject application. Applicants respectfully request the Examiner withdraw the rejection.

Rejection based on 35 U.S.C. 103. Claims are rejected under 35 U.S.C. 103(a) as being unpatentable over Haybittle as evidenced by Zhou in view of Augsburger in view of Smerhovsky as applied to claims 1-3 and 30 above, and further in view of Konno et al. ("Konno") (RETINA, vol. 21, pp. 57-61, 2001). Applicants traverse this rejection to the extent that it is maintained over the claims as amended.

Konno describes reproducibly measuring foveal thickness in healthy patients using optical coherence tomography (OCT) and scanning retinal thickness analyzer (RTA). Konno does not teach nor suggest a method for monitoring the effectiveness of a regimen for treatment of an ocular disease, comprising: (ii) treating said subject, or a different subject, with said

regimen for a selected period of time; (iii) obtaining from a subject who has been treated with the regimen, one or more measurements selected from self-reported date and behavioral, genetic, neurological, biochemical, and physiological measurements; (iv) determining changes in the measurements induced by the regimen, by comparing the measurements obtained prior to the regimen to (iii); (v) comparing said measurements or changes in the measurements, or both, to a signature, said signature representing probability relationships between one or more predictor variables and one or more clinical outcomes for said disease; and (vi) determining, from the comparison in (v), a probability that continued treatment of the subject with the regimen will result in a favorable clinical outcome. Konno is silent with regard to a regimen or treatment.

As discussed above, Haybittle as evidenced by Zhou in view of Augsburger in view of Smerhovsky does not teach a method for monitoring the effectiveness of a *regimen that is administered for a selected period of time* for treatment of an *ocular disease*, wherein a determination of a probability that *continued treatment of a subject with said regimen* will result in a favorable clinical outcome is made from a comparison of measurements taken before and after the treatment regimen. Konno, as outlined above, simply describes procuring measurements of foveal thickness in healthy patients using a different technology and is silent with regard to a regimen or monitoring the effectiveness of said regiment. Therefore, Haybittle as evidenced by Zhou in view of Augsburger in view of Smerhovsky in further view of Konno does not teach or suggest all of the claimed limitations of the subject application. Applicants respectfully request the Examiner withdraw the rejection.

Rejection based on 35 U.S.C. 103. Claims 1-5, 8-9, 12-13, and 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haybittle as evidenced by Zhou in view of Augsburger in view of Smerhovsky in view of Konno as applied to claims 1-5 above, in further view of Guo et al. ("Guo") (U.S. Patent 6,217,895). Applicants traverse this rejection to the extent that it is maintained over the claims as amended.

Guo describes a method for administering a corticosteroid to a posterior segment of an eye comprising implanting a sustained release device to deliver the corticosteroid to the vitreous of the eye and wherein aqueous corticosteroid concentration is less than vitreous corticosteroid concentration during release. Guo does not teach or suggest a method for monitoring the effectiveness of a regimen for treatment of a disease, comprising: (ii) treating said subject, or a

different subject, with said regimen for a selected period of time; (iii) obtaining from a subject who has been treated with the regimen, one or more measurements selected from self-reported date and behavioral, genetic, neurological, biochemical, and physiological measurements; (iv) determining changes in the measurements induced by the regimen, by comparing the measurements obtained prior to the regimen to (iii); (v) comparing said measurements or changes in the measurements, or both, to a signature, said signature representing probability relationships between one or more predictor variables and one or more clinical outcomes for said disease; and (vi) determining, from the comparison in (v), a probability that continued treatment of the subject with the regimen will result in a favorable clinical outcome. In fact, Guo is silent with regard to a disease or measurements from a subject.

As discussed above, Haybittle as evidenced by Zhou in view of Augsburger in view of Smerhovsky in view of Konno does not teach a method for monitoring the effectiveness of a *regimen that is administered for a selected period of time* for treatment of an *ocular disease*, wherein a determination of a *probability that continued treatment of a subject with said regimen* will result in a favorable clinical outcome is made from a comparison of measurements taken before and after the treatment regimen. While Guo teaches a method of administering a corticosteroid to a segment of an eye via implanting a sustained release device that delivers the corticosteroid, it does not teach the determination of a probability that *continued treatment will result in a favorable clinical outcome* (step vi). Therefore, Haybittle as evidenced by Zhou in view of Augsburger in view of Smerhovsky in view of Konno in further view of Guo does not even teach or suggest all of the claimed limitations of the subject application. Applicants respectfully request the Examiner withdraw the rejection.

Rejection based on 35 U.S.C. 103. Claims 31-34 are rejected under U.S.C. 103(a) as being unpatentable over Haybittle as evidenced by Zhou in view of Ando et al. ("Ando") (US PGPUB 2004/0039620). Applicants traverse this rejection to the extent that it is maintained over the claims as amended.

Haybittle describes a method for the study of prognostic factors (including age, menopausal status, tumor size and grade, and oestrogen-receptor (RE) content) in a series of 387 female patients afflicted with breast cancer and treated by a mastectomy and triple-node biopsy.

(Haybittle, abstract). Haybittle uses survival time of the patients as a measure of the outcome of the treatment. (Haybittle, p. 362, column 1). Measurements of these factors are taken before and after treatment. Data generated from this method is analyzed using a procedure described in Zhou. This analysis is used to derive a prognostic index (I) for each patient. These I values were then used to group patients with regard to their specific prognosis.

Conversely, the pending claims define a method for conducting a drug discovery business, comprising: (i) obtaining, from a test animal or from stored data, one or more measurements selected from behavioral, neurological, biochemical, and physiological measurements; (ii) treating said test animal with a test compound for a selected period of time; (iii) obtaining, from a test animal treated with the regimen, one or more measurements selected from behavioral, neurological, biochemical and physiological measurements; (iv) determining changes in the measurements induced by the regimen, by comparing the measurements obtained in (i) with the measurements, or both, to a signature, said signature representing probability relationships between one or more predictor variables and one or more clinical outcomes for said disease; and (vi) determining, from the comparison data of step (ii), the suitability of further clinical development of the test compound. Haybittle does not disclose or suggest treating a test animal with a test compound for a selected period of time. The only treatments disclosed in Haybittle are mastectomy, triple-node biopsy, and adjuvant chemotherapy. The latter is not even used in the determination of the Haybittle prognostic index.

Ando recites a profitability-evaluating system for a medical drug candidate under development, comprising a data set-creating subsystem and a management index-calculating subsystem, wherein said data set-creating subsystem includes a sales amount-estimating section for estimating sales amount of a product, a cost-estimating section for estimating an expense, A NPV-calculating section for calculating a cash flow and a net present value from an estimated sales amount and an estimated expense, and an IRR-calculating section for calculating an internal rate of return from the cash flow, an estimated investing amount, and a success probability, and a data set-recording section for recording the respective values determined by these estimating sections and calculating sections; and said management index-calculating subsystem includes an option value-calculating section for calculating the value of an option from the data set on the data set recording section, and a project value-calculating section for

calculating the value of a project of developing a medical drug from the value of the option. Ando is silent with regard to a test compound and a comparison of measurements taken from test animals for determining the further clinical development of the test compound.

As stated above, Haybittle does not teach treating a *test* animal with a *test compound* for a *selected period of time*. Adding Ando to Haybittle would not add any of the claimed subject matter that Haybittle lacks. Specifically, Ando makes no mention of treatment of a *test* animal with a *test compound*. In fact, Ando does not mention a treatment at all. Therefore, neither Haybittle nor Ando, taken separately or together, teach or suggest all of the claimed limitations of the subject application.

In addition, there is no motivation to modify Haybittle in light of Ando as outlined above and there is no reasonable expectation of success if the modifications are made. In Haybittle, the prognostic index is directed toward enabling the identification of a large group of patients with primary breast cancer that have a poor prognosis (Haybittle, abstract). The prognostic index was not developed within the context of finding a substance suitable for introduction as a clinical candidate. In fact, Haybittle is only directed toward a biopsy or mastectomy as possible treatments.

The method for conducting a drug discovery business in Ando is directed toward finding the profitability and market value of a possible drug by estimating sales amount, overhead costs, etc., e.g., the financial success of the treatment. It has nothing to do with determining the probability that a clinical candidate will be found safe or effective in clinical trials and ultimately admitted to the market, e.g., the therapeutic success of the treatment. Indeed, this probability is a variable used in Ando's method, but apparently must be calculated independently for use in Ando's method. The pending claims are directed to a method for evaluating therapeutic success, not financial success, and Ando is thoroughly irrelevant to this method.

One of ordinary skill in the art would not have had motivation or a reasonable expectation of success to modify Haybittle's teachings in light of Ando to obtain the claimed invention of the subject application. In fact, the combination of Haybittle and Ando does not even teach or suggest all of the claimed limitations of the subject application. Therefore, Applicants respectfully request the Examiner reconsider and withdraw the rejection.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617.951.7000. A two-month petition for extension of time and authorization of the prescribed fee are being filed herewith. Please charge any further fees due or credit any overpayments to our Deposit Account No. 18-1945, under Order No. CDSI-P01-020 from which the undersigned is authorized to draw.

Dated: June 7, 2007

Respectfully submitted,

By _____

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